I Rejections Under 35 U.S.C. § 101

The Examiner has rejected claims 23-54 under 35 U.S.C. § 101, as allegedly having no apparent or disclosed patentable utility. More specifically, the Examiner alleges:

> [t]he instant application does not disclose the biological role of this protein or its significance ... [t]he Specification sets forth that the CCIII is homologous to known proteins. However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors ... [a]fter complete characterization, this protein may be found to have a patentable utility ... [u]ntil some actual and specific significance can be attributed to the protein identified in the specification as CCIII, the instant invention is incomplete.

See, Office Action, at pages 3-4. Applicants respectfully disagree and traverse this rejection.

Applicants respectfully point out that the pending claims have previously been rejected as allegedly having no apparent or disclosed patentable utility. *See*, Paper No. 02052004, mailed February 19, 2004, at pages 6-9. Applicants Amendment and Reply under 37 C.F.R. § 1.111 filed May 14, 2004, contained a complete response to the Examiner's rejection and was accompanied by Exhibits A and B, which provided evidentiary support for Applicants assertion of utility. Having considered Applicants' Reply in light of the teachings of Exhibits A and B, the Examiner withdrew the rejection of these claims under 35 U.S.C. § 101 for alleged lack of patentable utility. *See*, Paper No. 07272004, mailed August 11, 2004.

A rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention, or statements made by the Applicants in the written description of the invention. *See* M.P.E.P. §§ 2107.01(II), (III) at 2100-[33-36] (Rev. 1, Feb. 2003). In addition, Applicants need only make *one* credible assertion of utility for the claimed invention to satisfy 35

U.S.C. § 101. *See, e.g., Raytheon v. Roper,* 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."). *See,* M.P.E.P. at 2100-33. Finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. M.P.E.P. § 2107.01(II)(B) at 2100-[33-34].

Moreover, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt *(i.e.,* "question") the truth of the statement of utility. M.P.E.P. § 2107.01(II) at 2100-[33-34]. Thus, the Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. *Id.* The Examiner must also present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicants' assertion of utility. *See id.*; *see also, In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). For the reasons set forth below, the Examiner has not met the burden that is necessary to establish and maintain a rejection for lack of utility under 35 U.S.C. § 101.

Contrary to the Examiner's comments, Applicants have set forth in the specification, a specific, substantial and credible utility which supports the claimed polypeptides of the present invention. In the specification at page 31, ¶157, Applicants teach that the invention is useful as a diagnostic reagent, for example, in the "diagnosis of a disease or susceptibility to a disease which results from under-expression over-expression or altered expression of CCIII, for example, neoplasia such as cancers and tumors." Therefore, Applicants submit that the specification clearly and specifically asserts a use for the claimed invention, *i.e.*, the diagnosis of cancers and tumors. The asserted utility for the claimed polynucleotides of the present invention is supported by post filing date

references to which the Examiner's attention is respectfully directed, and which are attached hereto as Exhibit A (Chien, W. and Pei, L. (2000) *J. Biol. Chem.* 275(25): 19422-19427), and Exhibit B (McCabe, C.J., *et al.* (2003) *Clin. Endocrinol.* 58(2): 141-150).

Chien and Pei (Exhibit A) disclose a polynucleotide which encodes the CCIII polypeptide of the present invention and identify this polynucleotide as "PTTG binding factor (PBF)". *See*, Exhibit A, page 19423. Chien and Pei demonstrate that "PBF" binds directly to Pituitary tumor-transforming gene (PTTG), a polypeptide believed responsible for tumorigenesis in the pituitary and various other tissues. *See*, Exhibit A, page 19422, and Figures 3-5 at pages 19423-19424. Chien and Pei further demonstrated that "PBF" binding is required for PTTG activation of transcription from the bFGF promoter. *See*, Exhibit A, Figure 9 at page 19426. The authors finally conclude that PBF binding to PTTG "suggest a potential mechanism by which PTTG might function as a transcriptional activator." *See*, Exhibit A, page 19427. Because the polypeptide identified by Chien and Pei as "PBF" is identical to CCIII of the present invention, and because the polypeptide identified by Chien and Pei as "PBF" is specifically required for the transcriptional activation activity of a known oncogene, the observations described above confirm Applicants' assertion of a specific utility that the CCIII polypeptides, antibodies and polynucleotides of the present invention will be useful in the diagnosis of cancers and tumors.

Furthermore, McCabe et al. (Exhibit B) demonstrate that expression of "PBF" was upregulated sixfold in pituitary tumors isolated from a large cohort of patients. See, Exhibit B at page 144, right column first paragraph; and page 145, Figure 2. McCabe et al. determine "[o]ur data support a fundamental role for PTTG-mediated upregulation of FGF-2 signalling in pituitary tumorigenesis." See, Exhibit A at page 141, right column lines 7-9. Because the polypeptide identified by McCabe et al. as "PBF" is identical to

CCIII of the present invention, because the polypeptide identified by McCabe et al. as "PBF" is upregulated in pituitary tumors, and because the polypeptide identified by McCabe et al. as "PBF" is required for PTTG activation of FGF transcription, the observations described above confirm Applicants' assertion of a specific utility that the CCIII polypeptides, antibodies and polynucleotides of the present invention will be useful in the diagnosis of cancers and tumors.

Thus, polynucleotides of the invention, together with polypeptides which they encode and antibodies specific for those polypeptides, may be used in the diagnosis of cancers such as, for example, pituitary cancer (*See, e.g.*, Specification at page 31, ¶157; and at page 34, ¶171). Applicants submit that, for example, the use of polypeptides, antibodies, or polynucleotides of the invention, in the detection of pituitary cancer, is a specific utility in that detection of this disorder is not possible with all polypeptides. This utility is also substantial in that improved detection of this disorder would substantially benefit patients and their healthcare providers throughout the world.

In light of the above facts, Applicants submit that one of ordinary skill in the art would have found the Applicants' asserted utility to be more likely than not true, and therefore the Applicants asserted utility is credible. Therefore, Applicants argue that the present invention meets the statutory utility requirement under 35 U.S.C. § 101, and as further described in the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Other than the conclusory statements that the invention lacks utility, the Examiner has presented no arguments as to why Applicants' asserted utility is not credible. In arguing that Applicants' asserted utility is not credible, the Examiner must attack (a) the logic underlying the assertion as seriously flawed or (b) the facts upon which the assertion is based as inconsistent with the logic underlying the assertion. *See*, Revised Interim

Utility Guidelines Training Materials, p. 5. In the instant rejection, the Examiner has set forth no arguments as to why Applicants' logic (that human CCIII may be used in the detection and/or diagnosis of cancers and tumors) is flawed or that the facts upon which the logic is based on, are inconsistent with the underlying assertion. Thus, the Examiner has failed to make even a *prima facie* showing that Applicants' asserted utility is not credible.

Applicants submit that the asserted utilities for human CCIII are specific and substantial ("the general rule [is] that the treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101." (Revised Interim Utility Guidelines Training Materials, p. 6)). In addition, Applicants submit that these utilities are credible. The Examiner has failed, however, to provide any countervailing statements as to why these particular utilities are not specific, substantial and credible.

Even assuming, *arguendo,* the Examiner has established a *prima facie* showing that the claimed invention lacks utility, Applicants respectfully submit that they have rebutted the Examiner's showing by proffering sufficient evidence to lead one skilled in the art to conclude that the asserted utilities are more likely than not true. Applicants have directed the Examiner to the specification where clear and specific assertions are made in support of patentable utilities of human CCIII and sequences of the present invention.

In view of the above, Applicants submit that the asserted utilities of the invention meet the statutory requirement set forth in 35 U.S.C. § 101. Accordingly, Applicants respectfully request that the rejection be withdrawn.

II Rejection Under 35 U.S.C. § 112, first paragraph

A. The Examiner rejects claims 23-54 under 35 U.S.C. § 112, first paragraph. Specifically, it is the Examiner's contention that claims 23-54 are "not supported by either a specific and substantial asserted utility or a well established utility for the reasons set

forth above, one skilled in the art clearly would not know how to use the claimed invention." *See*, Office Action, at page 5. Applicants respectfully disagree and traverse this rejection.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, Applicants respectfully assert that the claimed invention is supported by a specific and substantial asserted utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107.01 (IV) at 2100-[36-37]. Therefore, because the claimed invention complies with the utility requirement of 35 U.S.C. § 101, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention.

B. The Examiner has rejected claims 41-54 under 35 U.S.C. § 112, first paragraph, as allegedly failing to "reasonably provide enablement for a fragment of 30-50 contiguous amino acids of SEQ ID NO:2." More specifically, the Examiner alleges:

> [t]he claims are drawn to a fragment of the amino acid sequence of SEQ ID NO:2. Claims 41-54 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides will retain the characteristics of CCIII ... since Applicant has only taught how to test for polypeptide fragments of CCIII, and has not taught how to make polypeptide fragments of CCIII, it would require undue experimentation of one of skill in the art to make and use the claimed fragments.

See, Office Action, at pages 5-6. Applicants respectfully disagree and traverse the rejection.

Preliminarily, Applicants respectfully point out that pending claims 41-54 are directed to fragments of the polypeptides disclosed in the instant application. Indeed, the broadest rejected claims are directed solely to polypeptides "consisting of" at least 30

contiguous amino acids of the amino acid sequence of SEQ ID NO:2, and the amino acid sequence encoded by the cDNA contained in ATCC Deposit No. 97406. Therefore, rejection of the instant claims as lacking guidance concerning "the myriad of variant polypeptides" of the invention is unfounded.

Indeed the skilled artisan could clearly envision each of the claimed polypeptides consisting at least 30 contiguous amino acids of the defined amino acid sequence as a progression, *i.e.*, polypeptides comprising amino acids 1-30, 2-31, 3-32, etc. The skilled artisan could certainly further envision sequentially adding contiguous amino acids to either end of any of the described embodiments. Indeed, nothing more than what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides and polypeptide fragments containing at least 30 amino acids of SEQ ID NO:2 or encoded by the cDNA contained in ATCC Deposit No. 97406. Therefore, given the advanced state of the biochemical and molecular biological arts, the skilled artisan would have been able to make every one of the claimed polypeptides and polypeptide fragments using routine methods.

Furthermore, the skilled artisan would have been able to make each and every one of the claimed polypeptides using methods and techniques described in the specification and well known in the art. The specification teaches a number of methods for the expression of polypeptides, including, for example, those found in examples 1-3 at pages 44-50. One skilled in the art would have been capable of using routine techniques to design new polynucleotide primers, produce new expression vectors, and express each of the claimed polypeptides according to the methods described in these examples. Accordingly, nothing more than routine experimentation would have been required to make the claimed polypeptides.

It is well settled that the test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics, Inc.*, 857 F.2d 778, 8 U.S.P.Q. 2d 1217 (Fed. Cir. 1988). Under 35 U.S.C. § 112, enablement is not precluded even if some experimentation is necessary. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1376, 1384 (Fed. Cir. 1986). This is so even if the amount of experimentation required is laborious. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). Furthermore, enablement is not precluded even if some embodiments of the claimed invention are inoperative. Indeed, the M.P.E.P. states that "[t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled." *See*, M.P.E.P. § 2164.08(b).

Applicants assert that the Examiner has underestimated the level of skill of the skilled artisan, and that the skilled protein chemist or molecular biologist, enlightened by the teaching of the present specification, is more than capable of routinely making every polypeptide encompassed by the instant claims. Accordingly, one reasonably skilled in the art, armed with the disclosure in the present specification coupled with information known in the art at the time the application was filed, could make and use the claimed polypeptides, without undue experimentation. Therefore the claimed polypeptides are fully enabled within the meaning of 35 U.S.C. §112.

Applicants submit that because of: (1) the availability of routine techniques for synthesizing peptides; (2) the knowledge of the amino acid sequence of SEQ ID NO:2; (3) the availability of routine techniques for assaying for activity of the claimed polypeptides; (4) the high level of skill in the field of protein chemistry and molecular biology; and (5) the direction and guidance provided by the specification regarding the claimed

polypeptides and uses thereof, one skilled in the art could routinely generate the claimed polypeptides and confirm which of these exhibit functional activity.

In view of the above remarks, Applicants believe the Examiner's concerns have been fully addressed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 41-54 under 35 U.S.C. § 112, first paragraph, for lack of enablement.

Conclusion

In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: May 5, 2005

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